## REMARKS

Claims 10-45 are pending. Claims 10-18, 39-41 and 43 are under examination. Claim 40 has been amended. Support for the amendment to claim 40 can be found, for example, page 8, lines 21-22. Accordingly, the amendment does not raise an issue of new matter, and entry thereof is respectfully reqested.

Rejections Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 10-18, 40, 41 and 43 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description and as allegedly containing new matter is respectfully traversed. Applicants maintain that the specification as filed provides sufficient description of the recited terms alleged to be directed to new matter.

Applicants respectfully disagree with the assertion in the Office Action that the specification provides no indication that Applicants had possession of the concept of screening the claimed "collective ligand variant population" for binding against "two or more receptors" or "five or more receptors." The specification teaches that "a population of receptors can be screened with a ligand variant population" (emphasis added) (page 12, lines 25-29). The specification also teaches that a "population" refers to a "group of two or more different molecules" and can be between about 5 and 10 different molecules and up to hundreds or thousands of different molecules or even more (page 9, line 26, to page 10, line 7). Therefore, based on the teachings in the specification, one skilled in the art would readily understand that Applicants were in possession of the claimed methods that recite contacting a collective ligand variant population with a population of two or more or five or more receptors in view of the explicit teachings in the specification.

Furthermore, original claim 10 recites "contacting a collective ligand variant population with said one or more receptors." Thus, original claim 10 clearly recited contacting a collective ligand variant population with one receptor or more than one receptor. Accordingly, it would have been clear to one skilled in the art that a method of the invention included contacting "one or more receptors" and, based on the teachings in the specification that a population included "two or more molecules," it would also have been clear to one skilled in the art that more than one receptor encompasses two or more receptors, defined in the specification as a population.

As discussed in the previous response filed July 14, 2003, the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to a person skilled in the art that the inventor had possession of the claimed subject matter at the time of the filing date. In re Kaslow, 707 F.2d 1366, 217 U.S.P.Q. 1089 (Fed. Cir. 1983); Eiselstein v. Frank, 52 F.3d 1035, 34 U.S.P.Q. 2d 1467 (Fed. Cir. 1995). Based on the teachings in the specification, and as discussed above, Applicants respectfully maintain that the specification provides sufficient description and guidance for the recited phrases "two or more receptors" and "five or more receptors." Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 10-18, 39-41 and 43 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicants maintain, for the reasons of record, that the specification provides sufficient description and guidance for the claimed methods.

As discussed in previous responses with regard to the phrase "ligand variant population," the specification teaches that a ligand "variant" shares a similar structure and function (page 8, lines 26-28). In addition, the specification teaches that variants possess substantially the same or similar binding function as a parent molecule (page 8, lines 26-32). In contrast to the assertion in the Office Action that the claims encompass an infinite number of variations, the claimed population of variant ligands are related by structure and function.

The Office Action further alleges that the specification does not describe an example of a collective ligand variant population and that an example is required because the art is unpredictable. For the reasons of record, Applicants maintain that a working example is not required but, nevertheless, that the specification provides a working example that one skilled in the art would readily recognize as applicable to a variant ligand population. In particular, one skilled in the art would have readily understood that the description in Example V of antibody variant receptors and anti-idiotypic antibodies is applicable to ligand variants.

In the Office Action, it is indicated that the Examiner deems the art to be unpredictable. Furthermore, the Office Action indicates on page 8, paragraph 16, that adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled

in the art that compounds falling within the scope possess utility and demonstrate that Applicant was in possession of the claimed invention. The Office Action additionally asserts that "[T]he more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure." Applicant's representative is not aware of the precedent for such an assertion with respect to written description and would appreciate being provided with the relevant authority so that the case law can be reviewed and responded to appropriately.

Applicants maintain that the specification provides sufficient description and guidance to convey to one skilled in the art that Applicant was in possession of the claimed methods at the time the application was filed. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 10-18, 39-41 and 43 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Applicants respectfully maintain that the specification provides sufficient description and guidance to enable the claimed methods.

Regarding the alleged breadth of the claims as it relates to the structure of a collective ligand variant population and as discussed above, the specification teaches that the ligand variants share structural and functional properties similar to a parent molecule (page 8, lines 26-32).

Regarding the alleged unpredictability in the art, Applicants respectfully submit that the specification provides sufficient description and guidance to enable the invention as claimed. The Office Action acknowledges that ligand/receptor binding pairs were well-known in the art at the time of the invention, however the Office Action maintains that only limited numbers of such pairs were known. The assertion that only a limited number of ligand/receptor pairs were known at the time of filing the application is contrary to what was well known to those skilled in the art. Applicants have provided evidence in a previous response of numerous receptor/ligand pairs that were known at the time of filing the application (see in particular Exhibits B-D in the response filed February 15, 2002). The specification also exemplifies ligand/receptor pairs as antibodies and antigens. One skilled in the art would have been aware of the existence of hundreds to

thousands of ligand/receptor pairs and could have readily determined binding of ligand/receptor pairs based on the teachings in the specification and what was well known in the art.

Regarding unpredictability in the use of melanophore cells and adding tags to ligands, Applicants maintain, for the reasons of record, that the specification teaches routine methods of using melanophore cells to express variants (page 24, line 11 to page 25, line 32; Example I, pages 37-40) and routine methods for tagging with an identifiable tag (page 28, line 18 to page 30, line 24; and Example I, page 38, lines 18-33). Therefore, based on the teachings in the specification and what was well known to those skilled in the art, Applicants maintain that one skilled in the art would have readily been able to link a tag to a ligand variant and to use melanophore cells in the claimed methods.

Regarding the alleged unpredictability of adding tags to ligands, the Office Action cites an article by Janda (Proc. Natl. Acad. Sci. USA 91:10779-10785 (1994)) as describing the unpredictability of tagging methods. However, as discussed in the previous response mailed July 14, 2003, Applicants maintain that the article by Janda cites several references that have successfully used different tagging methods. Thus, Janda corroborates the teachings in the specification that one skilled in the art would readily understand how to tag a ligand variant population without undue experimentation.

With regard to the alleged lack of working examples, Applicants respectfully point out, as discussed above, that the specification provides a working example that one skilled in the art would readily understand is applicable to the claimed method in which a ligand variant population is contacted with a population of two or more or five or more receptors. Thus, Applicants respectfully maintain that the application provides sufficient description and guidance such that one skilled in the art could make and use the invention as claimed.

Applicants respectfully maintain that the specification provides sufficient description and guidance to enable the claimed methods. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 10, 17, 39 and 40 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. With regard to the term "tag," the Office Action indicates that claims 10, 17 and 39 recite that the ligand variants are tagged. It is respectfully pointed out that claim 10 does not recite the term "tag."

With regard to claims 17 and 39, these claims recite that the ligand variant is linked to a tag. The specification teaches that a tag can be used to facilitate the identification of a variant population (page 28, line 18, to page 30, line 24). The specification describes exemplary tags, including peptide tags and various methods of making such tags. Such methods include methods of generating mutations in a peptide sequence to generate a unique peptide recognized by a specific antibody (page 29, lines 1-14). The specification also exemplifies the use of a combination of peptides, each recognized by a specific antibody, to generate a large number of specific tags using a limited number of peptides recognized by specific antibodies (page 29, line 30, to page 30, line 4). The specification also describes how such tags can be used to identify a particular variant (page 30, lines 5- 24).

The Office Action indicates that it is unclear how polypeptide ligands are to be tagged with "peptide tags." Applicants respectfully maintain that one skilled in the art would have readily understood how a polypeptide ligand can be tagged with a peptide based on the teachings in the specification and what was well known to those skilled in the art for generating epitope tags, as disclosed in the specification. Therefore, Applicants respectfully maintain that the claimed methods reciting a ligand variant linked to a tag, including a peptide tag, would have been clear to one skilled in the art. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In the Office Action, claims 17 and 39 are indicated to be incomplete for "omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections," referring to MPEP § 2172.01. The Office Action asserts that the omitted structural relationships are how the claimed tags are associated with the ligands.

Applicant respectfully disagrees with the assertion that the claims omit essential cooperative relationships of elements. As discussed above, it is respectfully submitted that one skilled in the art would have understood how a tag can be linked to variant ligands and the relationship between the tag and the ligand variants.

With respect to the reference to MPEP § 2172.01, the section of MPEP § 2172.01 related to a rejection under § 112, second paragraph, refers to In re Venezia, 530 F.2d 956, 189 USPQ 149 (CCPA 1976) and In re Collier, 397 F.2d 1003, 158 USPQ 266 (CCPA 1968). It is respectfully pointed out that the issue in these cases was the relationship between a kit and a coaxial cable, respectively, and language in the claims related to the use of elements of the kit and coaxial cable. The CCPA found that language regarding the use of the components of the coaxial cable did not provide a positive recitation between two elements (In re Collier), whereas the components of the kit were viewed as definite (In re Venezia). It is respectfully submitted that the issues raised in In re Collier and In re Venezia are distinguishing features relevant to comparing the method claims of the present invention, which clearly recite the relationship between elements, as discussed above, and the apparatus and kit with tangible structural features at issue in In re Collier and In re Venezia.

Applicants respectfully submit that claims 17 and 39 are clear and definite. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The Office Action indicates that claim 40 is unclear for the recitation of the term "organic-derived compound ligands." Applicants maintain, for the reasons of record, that this term is clear and definite. Nevertheless, to further prosecution, claim 40 has been amended to recite the term "organic compound." Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 102

The rejection of claim 41 under 35 U.S.C. § 102(b) as allegedly anticipated by Combs et al., J. Am. Chem. Soc. 118:287-288 (1996), is respectfully traversed. Applicants respectfully maintain that claim 41 is novel over the Combs et al. reference. Applicants maintain that Combs et al. does not teach contacting a collective ligand variant population with a population of two or

more receptors, but rather describes ligands that were contacted with one "receptor" (SH3 domain from Src), and subsequently one ligand (ligand 1A) was contacted with another "receptor" (SH3 domain from the p85 component of PI3K) (see, for example, Combs et al., page 288, 2nd paragraph, 1st sentence).

Thus, the Combs et al. reference does not teach the claimed method and, therefore, this reference cannot anticipate claim 41. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 10-14, 17, 18, 40 and 43 under 35 U.S.C. § 103 as allegedly obvious over Combs et al., *supra*, is respectfully traversed. Applicants maintain that these claims are unobvious over Combs et al.

As described above, Applicants maintain that the Combs et al. reference does not teach or suggest the contacting of a collective ligand variant population with a population of two or more or five or more receptors, but rather in the reference by Combs et al., ligands were contacted with one "receptor" and subsequently one ligand was contacted with another "receptor." Thus the publication by Combs et al. cannot render the claimed invention obvious. Accordingly, Applicants respectfully request that this rejection be withdrawn.

## CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned attorney if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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